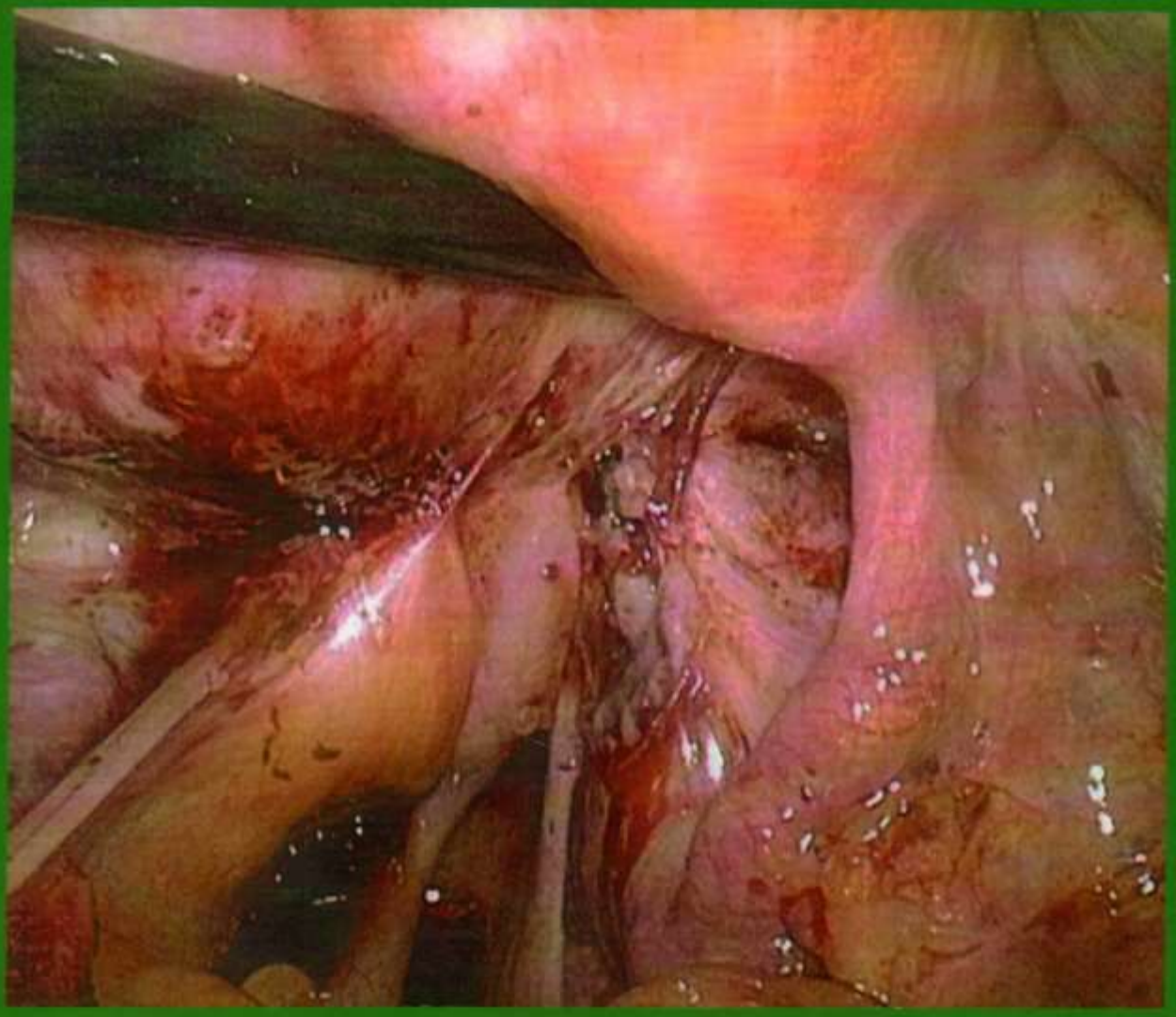
Majalah Obstetri & Ginekologi



MOG	Vol. 19	No. 3	Hlm. 96-139	Sep - Des 2011	ISSN 0854-0381

Vol. 19 No. 3 September – Desember 2011 ISSN 0854-0381

Majalah Obstetri & Ginekologi

SUSUNAN PENGURUS MAJALAH OBSTETRI & GINEKOLOGI

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Vol. 19 No. 3 September – Desember 2011 ISSN 0854-0381

Majalah Obstetri & Ginekologi

DAFTAR ISI

Gambar sampul depan :
Endometriosis Spot
http://womenshealthtoday.files.wordpress.com/2009/10/02a_adhesion.jpg

PEDOMAN PENULISAN NASKAH

Majalah Obstetri & Ginekologi menerima naskah asli berupa hasil penelitian, laporan kasus, atau tinjauan pustaka yang merupakan konsep-konsep pemikiran inovatif hasil telaah pustaka yang bermanfaat untuk menunjang kemajuan ilmu, pendidikan, dan praktik obstetri dan ginekologi. Redaksi hanya menerima naskah asli yang belum pernah dipublikasikan di dalam maupun di uar negeri. Naskah dapat ditulis dalam bahasa Indonesia atau bahasa Inggris.

PEDOMAN UMUM

Naskah yang diserahkan kepada redaksi hendaknya mengikuti ketentuan-ketentuan sebagai berikut:

1. Naskah diketik pada lembar kertas A4, spasi 1,5 dengan jarak tepi kiri, atas, dan bawah masing-masing 3 cm serta kanan 2,5 cm. Setiap naskah ditulis dengan huruf Times New Roman dan tidak melebihi 10 halaman. Print out naskah dibuat rangkap tiga dan dilengkapi dengan file soft-copy dalam CD.
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3. Nama-nama Penulis, disertai informasi tentang identitas penulis, meliputi instansi tempat penulis bekerja dan alamatnya dengan jelas.
4. Abstrak (abstract), ditulis dalam Bahasa Inggris, tidak lebih dari 250 kata, dan merupakan intisari seluruh tulisan, meliputi: latar belakang, tujuan, metode dan hasil (untuk laporan penelitian), atau laporan kasus (untuk studi kasus), atau telaah pustaka (untuk tinjauan pustaka) dan diskusi (termasuk kesimpulan). Di bawah abstrak disertakan 3-5 kata kunci (key words).
5. Kutipan dalam naskah ditandai dengan mencantumkan nomor yang ditulis superskrip sesudah tanda baca. Setiap pustaka yang dikutip diberi nomor urut sesuai dengan urutan pemunculannya dalam naskah.

   Contoh penulisan kutipan dalam naskah:
   Pengalaman studi operasional Pelayanan Kesehatan Ibu berbasis-risiko berbasis-keluarga[1,2] dalam upaya pencegahan dan penurunan kematian ibu/bayi baru lahir di beberapa kabupaten .....
   Target nasional adalah menurunkan AKI menjadi 125/100000 KH di tahun 2010.[3] Untuk mencapai Indonesia Sehat tahun 2010 telah dikembangkan.....
   Menurut Azwar[3] ....

6. Ucapan terima kasih, dapat ditujukan pada semua pihak yang membantu bila memang ada, misalnya penyandang dana penelitian, dan harus diterangkan sejelas mungkin. Diletakkan pada akhir naskah, sebelum daftar pustaka.
7. Daftar Pustaka, disusun menurut sistem Vancouver (Sistem Nomor). Nomor setiap pustaka yang dirujuk dalam naskah disusun berurutan sesuai dengan urutan pemunculannya dalam naskah.

   Contoh penulisan daftar pustaka:
   1. Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002 Jul 25;347(4):284-7.
   2. Rose ME, Huerbin MB, Melick J, Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6.
   3. Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.
   4. Gilstrap LC 3rd, Cunningham FG, VanDorsten JP, editors. Operative obstetrics. 2nd ed. New York: McGraw-Hill; 2002.
   5. Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.
   6. Amerongen AVN, Michels LFE, Roukema PA, Veerman ECI. 1986. Ludah dan kelenjar ludah arti bagi kesehatan gigi. Rafiah Arbyono dan Sutatmi Suryo. Yogyakarta: Gadjah Mada University Press; 1992. h. 1-42.
   7. Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.
   8. Harnden P, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ Cell Tumour Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer; 2002.

   Nama penulis (author) ditulis semua, kecuali apabila lebih dari enam penulis, maka yang ditulis hanya enam nama dan diikuti dengan et al. Sebaiknya pustaka yang digunakan adalah yang paling mutakhir (diterbitkan dalam satu decade terakhir). Untuk pustaka/buku

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Naskah hasil penelitian hendaknya disusun menurut sistematika sebagai berikut: judul, nama penulis, identitas penulis, abstrak, pendahuluan, bahan dan metode, hasil dan pembahasan, kesimpulan, dan daftar pustaka.

1. Pendahuluan, meliputi latar belakang masalah, rumusan masalah serta tujuan penelitian dan manfaat untuk waktu yang akan datang.
2. Bahan dan Metode, berisi penjelasan tentang bahan-bahan dan alat-alat yang digunakan, waktu, tempat, teknik, dan rancangan percobaan. Hendaknya dijelaskan dalam bentuk esai bukan numerik. Metode harus dijelaskan selengkap mungkin agar peneliti lain dapat melakukan uji coba ulang. Acuan (referensi) diberikan pada metode yang kurang dikenal.
3. Hasil dan Pembahasan, hasil dikemukakan dengan jelas bila perlu dengan tabel, ilustrasi (gambar, grafik, diagram) atau foto. Hasil yang telah dijelaskan dengan tabel atau ilustrasi tidak perlu diuraikan panjang-lebar dalam teks. Persamaan Matematis dikemukakan dengan jelas. Jika simbol matematis tidak ada pada word proccesor dapat ditulis menggunakan pensil/pena dengan hati-hati. Kalau perlu beri keterangan simbol dengan tulisan tangan (pensil tipis). Angka desimal ditandai dengan koma untuk Bahasa Indonesia dan titik untuk bahasa Inggris. Tabel, ilustrasi atau foto diberi nomor dan diacu berurutan dengan teks, judul ditulis dengan singkat dan jelas. Keterangan diletakkan pada catatan kaki, tidak boleh pada judul. Semua singkatan atau kependekan harap dijelaskan pada catatan kaki. Pembahasan, menerangkan hasil penelitian, bagaimana hasil penelitian yang dilaporkan dapat memecahkan masalah, perbedaan dan persamaan dengan penelitian terdahulu serta kemungkinan pengembangannya.
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Naskah tinjauan pustaka disusun menurut sistematika sebagai berikut: judul, nama penulis, identitas penulis, abstrak, pendahuluan, telaah pustaka, pembahasan, kesimpulan, daftar pustaka.

PEDOMAN PENULISAN LAPORAN KASUS

Naskah laporan kasus disusun menurut sistematika sebagai berikut: judul, nama penulis, identitas penulis, abstrak, pendahuluan, kasus, tata laksana kasus seyogianya disertai dengan foto, pembahasan, kesimpulan, daftar pustaka.

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MANUSCRIPT PREPARATION GUIDELINES

Majalah Obstetri & Ginekologi publishes original articles on all aspects of obstetrics and gynecology. Articles can be classified as research reports, case reports and literature reviews that keep the readers informed of current issues, innovative thinking in obstetrics and gynecology. Articles are considered for publication with the condition that they have not been published or submitted for publication elsewhere. Manuscript should be written in English or in Indonesian. Authors should follow the manuscript preparation guidelines.

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The manuscript should follow the following guidelines:

1. The manuscript should be submitted in a compact disc. Three legible photocopies or an original plus two legible copies of manuscript typed 1.5 space (with wide margins: left, top and bottom 3 cm, right 2,5 cm) on good quality A4 white paper (210 x 297 mm) should be enclosed. The length should not exceed 10 pages and written in Times New Roman font.
2. Title, should be brief, specific and informative. Suggested not more than 12 words and does not contain any uncommon abbreviations. Include a short title (not exceeding 40 letters and spaces).
3. Name of Author(s), should include full names of authors, address to which proofs are to be sent, name and address of the Department(s) to which the work should be attributed
4. Abstract, concise description (not more than 250 words) of the purpose, methods and results (for research report), or case management (for case report), or literature study (for literature review) and discussion (including conclusions). Key words (3-5 words) should be provided below the abstract.
5. Citation should be identified in the text by the superscript Arabic numerals and numbered in consecutive order as they are mentioned in the text.

   Examples for citation writing:
   Pengalaman studi operasional Pelayanan Kesehatan Ibu berbasis-risiko berbasis-keluarga[1,2] dalam upaya pencegahan dan penurunan kematian ibu/bayi baru lahir di beberapa kabupaten .....
   Target nasional adalah menurunkan AKI menjadi 125/100000 KH di tahun 2010.[3] Untuk mencapai Indonesia Sehat tahun 2010 telah dikembangkan.....
   Menurut Azwar3 ....
6. Acknowledgments, to all research contributors, if any, should be stated in brief at the manuscript, prior to references
7. References, should be arranged according to the Vancouver system (Numerals system). The reference list should appear at the end of the articles in numeric sequence.

   Examples for references:
   1. Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002 Jul 25;347(4):284-7.
   2. Rose ME, Huerbin MB, Melick J, Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6.
   3. Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.
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   6. Amerongen AVN, Michels LFE, Roukema PA, Veerman ECI. 1986. Ludah dan kelenjar ludah arti bagi kesehatan gigi. Rafiah Arbyono dan Sutatmi Suryo. Yogyakarta: Gadjah Mada University Press; 1992. h. 1-42.
   7. Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.
   8. Harnden P, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ Cell Tumour Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer; 2002.

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3. Results and Discussion, results should be presented in logical sequence with the minimum number of tables and illustrations necessary for summarizing only important observations. Mathematical Equations, should be clearly stated. When mathematical symbols are not available on the typewriter, hand written symbols with soft lead pencil could be used. Decimal numbers, should be separated by point (.) for English-written-manuscript, and be separated by comma (,) for Indonesian-written manuscript. Tables, illustration, and photographs should be cited in the text in consecutive order. The titles and detailed explanations of the figures belong in the legends for illustrations (figures, graphs) not on the illustrations themselves. Explain in footnotes all nonstandard abbreviations that are used. Discussion, explaining the meaning of the examination's results, in what way the reported result can solve the problems, differences and equalities with previous study and development possibilities.
4. Conclusion, is the answer of the question and the purpose of research, its validity can be responsible, mentioned in the simple and clear sentences. Conclusion is not rewrite form of statistical test result.

LITERATURE REVIEWS PREPARATION GUIDELINES

The text of literature reviews should be divided into the following sections: title, name of Author(s), abstract, introduction, overview, discussion, conclusion, references.

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The Effect Of Curcumin to the Anti Mullerian Hormone Serum Concentration in Endometriotic Rat Model

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Dr. Soetomo Hospital, Surabaya

ABSTRAK

Terapi medis endometriosis hanya dapat digunakan dalam waktu yang terbatas karena timbul efek samping. Salah satu metode pengobatan yang dikembangkan untuk terapi medis tersebut adalah dengan menggunakan bahan-bahan herbal, antara lain kurkumin. Tujuan dari penelitian ini adalah untuk mempelajari konsentrasi AMH dalam serum dari model tikus endometriotik dengan suplementasi kurkumin. Penelitian eksperimental dilakukan pada laboratorium embriologi Fakultas Kedokteran Hewan Universitas Airlangga, Surabaya, Juli-Oktober 2011. Ini adalah tes laboratorium menggunakan 38 tikus betina (Rattus novergicus) yang tak sesuai kriteria inklusi. Untuk membuat model tikus endometriotik, masing-masing tikus disuntik dengan: A cyclosporin dan ethynil estradiol intramuskuler, jaringan endometrium manusia jinak intraperitoneal ovarium tumor. Model tikus endometriotik secara acak dibagi menjadi dua kelompok. Kelompok intervensi diberi kurkumin 24 mg (240 mg/kg) sekali sehari sampai empat belas hari. Tikus-tikus dikorbankan dan konsentrasi AMH dari serum diukur dengan alat tes ELISA kit dari Cusabio Biotech, Wuhan, Cina. Ada perbedaan yang signifikan pada konsentrasi serum AMH antara kurkumin kelompok (44.9 ± 20.1) kelompok plasebo (29.8 ± 11.9) (p <0.05). Sebagai kesimpulan, konsentrasi serum AMH lebih tinggi dalam model tikus endometriotik dengan suplementasi kurkumin. ***(MOG 2011:19;96-101)***

Kata kunci: *kurkumin, endometriosis, hormon anti-Mullerian*

ABSTRACT

Medical therapy of endometriosis can only be used within a limited time because of arising side effects. One method of medical treatment that was developed for this purpose is using herbal ingredients, the curcumin. The objective of this study was to study the AMH concentration in serum of endometriotic rat model with curcumin supplementation. This experimental study was performed at embryology laboratory Faculty of Veterinary Medicine of Airlangga University, Surabaya, July – October 2011. This was an experimental laboratory tests using 38 female rats (Rattus novergicus) with the inclusion criteria. To make endometriotic rat model, each rat was injected with: both cyclosporin A and ethynil estradiol intramuscularly, human endometrial tissue of benign ovarian tumors intraperitoneally. The endometriotic rat model were randomly divided into two groups. The intervention group was comsuming curcumin 24 mg (240 mg/kg) once daily until fourteen days. The rats were sacrificed and the AMH concentration from serum were measured by ELISA kit assay from Cusabio Biotech, Wuhan, China. There was a significant difference in serum concentration of AMH between curcumin group (44.9 ± 20.1) an placebo group (29.8 ± 11.9) (p < 0.05). In conclusion, the concentration of serum AMH is higher in endometriotic rat models with curcumin supplementation. ***(MOG 2011:19;96-101)***

Keywords: *curcumin, endometriosis, anti mullerian hormone*

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INTRODUCTION

Endometriosis is a disease that remains a problem for women of reproductive age. The prevalence in the general population of reproductive-age women between 3-10%.[15] Generally they are visiting a doctor with chief complaints of chronic pelvic pain, dysmenorrhoe, dyspareuni, and infertility. Data on dr.Soetomo Hospital Surabaya showed the incidence of endometriosis during laparoscopic procedure in patient with infertility, namely in 1987 and 1991 of 23.8%, in 1992 to 1993 increased to 37.2%, and the last in 2002 reached 50%.

There are several factors that cause high rates of infertility in patients with endometriosis, mechanical factors that cause adhesions of the reproductive organs and disrupt oocyte retrieval by fimbria during ovulation, another factors are defects of the immunological response and oocyte quality degradation due to interference folliculogenesis process. This decline in oocyte quality

will lead to low rates of pregnancy in women with endometriosis to less than 35% and the high incidence of abortion up to 27%.

Defective immunological response characterized by an increase in the inflammatory process induced by the activity of macrophages in the peritoneal fluid, macrophages will secrete excessive number of cytokines including TNF-α. TNF-α will diffuse into the follicle, then through binding to its receptor (TNF-R1) on the membrane of granulosa cells, TNF-α activates the cell death signals and induce the occurrence of the caspase cascade and stimulate the process of apoptosis in granulosa cells. TNF-α also increases the production of ROS via the JNK-1 and will increase the oxidative stress that stimulates the process of granulosa cell apoptosis.[1] These pathological process of apoptosis will cause interference with the function of granulosa cells. Has been demonstrated in previous studies that the folliculogenesis process obtained cooperation between granulosa cells and oocyte cells.[3] Both of these cells communicate with each other through paracrine pathways to produce good quality oocytes for fertilization, so that if an interruption occurs in granulosa cell function may result in decreased quality of oocytes and increased rates of infertility in patients with endometriosis.

Commonly therapies used in endometriosis is by surgery or medically with hormonal medication or combination of both. The basic principle of therapy is to suppress symptoms and prevent progression to reduce endometriosis implants. Cure rate of surgical therapy about 80%, but surgery is too invasive and the number of recurency about 10%-20% and still require additional therapy. Some hormonal therapies currently used are to inhibit the growth of endometriosis implants by pressing the steroid hormone released by the ovaries and cause hipoestrogenik circumstances. Medical therapy of endometriosis can only be used within a limited time because of side effects arising hipoestrogen, so people expected on the new problem of infertility. The high recurrence rate reached 45% after completion of medical therapy is still an issue today.

In line with the above conditions, the scientists tried to find new therapies with different molecular targets, has a high effectiveness and fewer side effects. One method of medical treatment that was developed for this purpose is using herbal ingredients that is curcumin. Curcumin is the active ingredient extracted from
Curcuma longa, called turmeric in English and in Indonesian called *kunir*. Curcumin is known to suppress mutagenesis and used as a chemopreventive agent for various cancers such as colon, breast, prostate, esophagus, lung, and inhibiting atherosclerosis, inhibits the growth of viruses and bacteria. Curcumin also has anti-inflammatory effects through suppression of activation of nuclear factor-κB (NF-κB), anti-proliferative effects through suppression of cyclin D1 and antiapoptotic gene product, induces release of cytochrome C and has the effect of anti-angiogenesis. [12] and also known to have antioxidant effects.[13]

In previous research has demonstrated that curcumin inhibited the growth of endometriosis cells via suppression of expression of VEGF (vascular endothelial growth factor) and a study by Johari[8] has shown that curcumin can increase the number and maturation of ova in mice endometriosis model performed ovarian stimulation through suppression of inflammatory processes curcumin can suppress angiogenesis factor VEGF and widespread endo-metriosis implants in mice model of endometriosis is comparable with progestin (MPA).

One marker that can be used to determine the function of granulosa cells was AMH (anti-Mullerian hormone) or MIS (müllerian inhibiting substance) which is a dimer glikoproterin included in the transforming growth factor-beta (TGF-ß) superfamily. AMH in women is produced by the granulosa cells of pre-antral follicles and antral who played a role in folliculogenesis.[16] AMH is secreted by the ovaries into the circulation so it can be measured in serum.

The levels of serum AMH in patients with endometriosis has found decrease and proportional to the degree, the more severe the levels of AMH are also on the downside as well as on the levels of AMH in follicular fluid.[3] AMH has advantages in describing the function of granulosa cells because it is not influenced by the menstrual cycle and use of contraceptive drugs, so it can be measured at each phase.

AMH is a fairly good marker as a prognostic value in predicting number of mature oocytes obtained in an assisted reproductive technologies (ART) after gonadotropin stimulation. AMH even has a better prognostic value than other markers such as FSH, inhibin B, and estradiol. AMH serum level is important for predicting response to ovarian endometriosis in women who followed the ART program. Expected if obtained AMH levels are high then the success rate of ART program is also expected to rise.

The following research proposes that granulosa cell apoptosis that occurs due to an increase in inflammatory factors in endometriosis will cause a decrease in AMH

levels. Expected with the administration of curcumin can inhibit inflammatory processes and apoptosis so as to suppress granulosa cell dysfunction characterized by high levels of AMH. With high levels of AMH are also expected to increase fertility.

MATERIALS AND METHODS

Animals used in this researcg were 38 mature female rats (*Rattus novergicus*), weighing 100-150 g. Animals were kept in cages in a well environment and has adaptated for 1 week. The fresh humans endometrial tissues was obtained from women undergoing elective hysterectomy for benign gynecological disease. The endometrial tissues then washed twice with phosphatebuffered saline (PBS) then suspended as coarse fragments in PBS with 200 IU/ml of penicillin and 200 µg/ml of streptomycin. Endometrial tissues then injected intraperitoneally using 16G neddle in rats. After injection of cyclosporin A and injection of estradiol on day 1 and day 5, the sampels then divided into two groups. Began the day-14 group A received curcumin per sonde during 14 days, while group B received placebo for 14 days per sonde. The rats then sacrificied at day 28 using high concentration of ether in a closed chamber.

The AMH concentration from serum were measured by ELISA kit assay for rat from Cusabio Biotech, Wuhan, China. Absorbance was measured at wavelength 450 nm by using a multiplate reader. The AMH result was calculated using the standard curve with a base value of the manufacturer's standard assay kit (Cusabio Biotech), and data are presented as ng/ml. Statistical analysis was perform using SPSS program (version 19.0.1). Before statistical analysis, the data conducted KolgomorovSmirnov normality test. If the normality test results are normally distributed, then proceed with parametric statistical tests of comparison of the mean of two groups using independent two-sample t test.This study uses a significance level of 0.05.

RESULTS AND DISCUSSION

The weight variable are analyze using the test for normality of distribution by Kolmogorov-Smirnov test. The curcumin group obtained $p = 0.416$ (before treatment) and $p = 0.712$ (after treatment). Similarly, in the placebo group, $p = 0.787$ obtained (before treatment) and $p = 0.711$ (after treatment). Since $p > 0.05$ then the two groups of normally distributed. Because the distribution is normal, then performed independent two-sample t test, and the obtained $p > 0.05$ in both groups so that it can be concluded that there was no significant differences. Similarly, the change in weight between the two groups, obtained $p > 0.05$, so no significant differences found in both groups and both groups are said to be homogeneous. Because the body weight of rats is homogeneous then the BB variables were not included in subsequent analysis.

Variable levels of serum AMH Normality was tested using Kolmogorov-Smirnov one sample, where the obtained $p = 0.061$ ($p > 0.05$), mean normal distribution. Because normally distributed, statistical tests used is parametric test using independent two-sample t test. Two-sample t test results obtained $p = 0.008$ ($p = 0.05$) which means the average obtained significant differences between groups of AMH serum levels of curcumin and placebo groups.

Endometriosis model made in rat does not fully represent the state of endometriosis in humans. But the endometrial-like lession resulting from the manufacture of this model is most similar to endometriosis cells in humans in terms of morphology and histopatology, so the state is considered to adequately represent the experimental model.

Making a rat model of endometriosis performed by lowering the immune response function artificially, ie suppress lymphocyte proliferation and differentiation using cyclosporine A (an immunosuppressant). Furthermore, extracts of human endometrial cells injected into the abdominal cavity of mice. Inflammat-ory process is expected to occur due to the inclusion of foreign objects into the abdominal cavity of mice.

This process will take about 3-6 days, then continued proliferation phase that aims to form granulation tissue. Intramusculus estrogen injection is used to enable the proliferation and growth of endometrial tissue in the abdominal cavity. Granulation tissue formation lasted until day 14, the process can continue until day 28. On day 14, treatment of curcumin and placebo on the rat model endometrosis begins. We did not conduct the confirmation incidence of endometriosis in macroscopic or histopathology specimens, therefore the success rate refers to the incidence of endometriosis is based on previous studies conducted by Kuswojo and Sa'adi.[9]

In this study we have found that although a statistically significant difference in mean AMH levels in both groups, but we see that the results in each group is not uniform. In the curcumin group, we still get a sample with low levels of serum AMH, as well as in the placebo group,

we still get the serum AMH levels are quite high. This possibility can be explained by previous studies by Grummer et al.[6] that it is influenced by the ability of rat model of recovery by itself. It is said that the ability of recovery varies between individuals and does not exceed the figure of 30%. This needs to be considered in analyzing the results of research, remember when we would do certain drug trials, because of differences in the number of lesions in both groups of experimental animals can be caused by differences in recovery at the beginning of the experiment compared the effects of the drugs tested. In this study, we divided rats randomly into 2 groups: group by treatment with curcumin supplementation and one group with placebo supplementation treatment (NaCl fluid).

It is therefore worth nothing that the study sample characteristics affect the results of the study, namely age and body weight of rats. We used female rats of the same age that is 3 months. At this age, rat are considered sexually mature so it is considered the same hormonal status. We did not do a vaginal smear to see the estrous cycles of rat when began the treatment or when taking a blood sample because it has been demonstrated by Aoki et al.[2] that the growth of endometrial cells that transplanted into SCID mice is not affected by the estrous cycle of mice, thereby allowing endometrial tissue transplants done at all estrous cycle of rats. AMH levels in human are not influenced by the menstrual cycle and use of contraceptive drugs, so it can be measured at each phase of the menstrual cycle, therefore the measurement of serum AMH levels in rats in our research is also considered to be unaffected.

Body weight of rats on our research about 100-150 grams. We measured body weight of rats at random. Body weight of rats we are testing with one sample Kolmogorov Smirnof, it obtained a normal distribution. After that we did a statistical analysis by independent two-sample t test and not found significant differences in body weight measurements before and after treatment as well as on changes in body weight in both groups ($p > 0.05$) so that the variable weight is homogeneous. In comparison there are few human studies that connecting between body mass index (BMI) and endometriosis. BMI in 366 women with endometriosis was lower than 268 women who underwent laparoscopy because of other minor gynecological problems. There is relationship between the degree of endometriosis with a BMI of women with endometriosis. In women with severe endometriosis degrees obtained a lower BMI compared with mild or moderate degree. We analogy there are similarities between the calculation of body weight of rats with BMI measurements in humans, so as a result we consider homogeneous then it is likely that the degree of endometriosis are positive in both groups was similar. Meanwhile, the study by Freeman et al.[5] found that in women who are obese have a lower AMH levels than non-obese, because the weight of rats homogeneous, we consider the differences in levels of serum AMH in our research not affected by body weight of rats.

Until now the method of treatment for endometriosis in humans is still not give encouraging results. One problem is the fear of side effects arising from such treatment, for example due to the effects of GnRH agonists hipoestrogenik or hiperandrogen effects on danazol administration. Thought that it tries to be developed is an attempt to discover new drugs that do not inhibit the hypothalamic-pituitary-ovarian, so people are not faced with infertility problems. One alternative that could be used is the use of curcumin herbal medium.

A mixture of several drugs including curcumin has the same safety and efficacy compared gestrinone in the prevention of recurrence in patients with endometriosis post-surgery. One mechanism is believed to be the effect of curcumin here is the suppression of proinflammatory cytokines, inhibition of COX-2 and antioxidant effects.[17]

Several studies have proven the cause of increased apoptosis in endometriosis is stimulated by increased pro-inflammatory cytokines, including the widely studied is TNF-α. Found an increase in TNF-α in both the fluid and follicular fluid peritoneum. Research by Hendarto[7] have elevated levels of TNF-α in the fluid peritoneum endometriosis women and the increase is in accordance with the degree of endometriosis. The higher the rank the levels of TNF-α is increasing. While the study by Falconer et al.[4] found levels of TNF-α in follicular fluid of endometriosis women taller than women infertile due to tubal factor.

Molecular mechanisms that could explain the involvement of TNF-α in the process of apoptosis is due to activation of one transcription factor NF-Kß is. Studies in vitro showed activation of NF-Kß in endometriosis stromal cells via the classical pathway of NF-Kß induced by IL-1. TNF-α or lipopolysaccharide.[11] NF-Kß transcription factor known to play a role in the pathogenesis of endometriosis, which stimulate the process of adhesion, invasion, angiogenesis, inflammation, proliferation, and inhibits cell apoptosis endometriosis. The role of classical pathway activation of NF-Kß is a natural immune response that stimulates inflammation and maintain endometriosis lesions.[11]

Activation of transcription factor NF-Kß is also associated with increased ROS (Reactive Oxygen Species). There is an increase in ROS in the stromal and epithelial cells from endometriomas and endometrium of endometriosis women. ROS are the main ingredients of superoxide (O2-) is converted to H2O2 by the enzyme SOD (super oxide dismutase), can further form hydroxyl Radicals (OH) ions due to the influence of H2O2 Fenton or Haber-Weiss reactions of O2. Hydroxyl Radicals have a short half-life and is much more reactive than superoxide. Schreck et al. (1991) proved H2O2 activates transcription factor NF-KB. H2O2 causes the release of NF-KB binding to IκB.

In several studies have demonstrated a decrease in both serum AMH levels in follicular fluid and endometriosis women. The study by Lemos et al.[10] obtain serum levels of AMH in women endometriosis was lower than that of control women with infertility due to tubal factor (1.26 ± 0.7 vs. 2.02 ± 0.72 with p = 0.004). Research by Shebl[14] also show decreased levels of serum AMH in women endometriosis compared to controls (husband factors) and increases with the degree of endometriosis, in women with mild endometriosis obtained mean AMH levels do not differ from controls (3.28 ± 1.93 vs 3, 44 ± 2.06, p = 0.61) in women with severe degrees obtained mean AMH levels are significantly different (2.38 ± 1.83 vs. 3.58 ± 2.46, p <0.0001).

While the study by Falconer et al.[4] find evidence of decreased levels of AMH in follicular fluid of endometriosis women. The mechanism of decrease in AMH levels has not been fully explained, this is likely to be influenced elevated levels of TNF-α in follicular fluid of endometriosis women, which ultimately induces an increase in the apoptotic process in granulosa cells. AMH levels decrease is probably caused by a reduced number of granulosa cells in cumulative result of an increase in the apoptotic process. However, this requires further research to prove it.

In our study, mean AMH levels in the rat model of endometriosis curcumin group higher than the placebo group (44.9 ± 20.1 vs. 29.8 ± 11.9). Based on two samples independent t test found significant differences between the two groups (p = 0.008). Difference in results is likely due to the success of curcumin in inhibiting the apoptotic process that occurs, as for the mechanism could be through multiple pathways including inhibition of activation of the transcription factor NF-Kß by a variety of consequences, suppression of inflammatory activity through the suppression of TNF-α directly or through antioxidant effect.

Curcumin can inhibit the activation of the transcription factor NF-Kß to the target before the phosphorylation Ißa emphasis. Curcumin was shown to reduce negative impacts resulting from endometriosis patients with immune defects by anti TNF-α, anti-NF-Kß, antioxidant, anti-JNK and anti-caspase activation pathway. Curcumin can suppress NF-KB pathway and NF-KB target genes cytokines.

Curcumin also has strong antioxidant capabilities. TNFα alone induces the formation of oxidative stress via JNK-1 pathway that ultimately can induce apoptosis process.[1] Curcumin has anti-oxidant effect and this has been demonstrated in several studies. Curcumin inhibits formation of hydroxyl Radicals (OH) from Fenton reaction or Haber-Weiss by increasing the activity of antioxidants such as SOD, GPX, GSH, and GST. Similarly, the chain termination or chain addition of hydrogen on the phenolic structure of materials can catalyze hydrogen peroxide (H2O2) into H2O and O2. Curcumin is an antioxidant by breaking the chain of exogenous oxidants that inhibit lipid peroxidation.

With inhibition of apoptosis that occurs will cause the number of granulosa cells that survived became higher so that proteins and hormones are secreted also higher. With more number of granulosa cells that survived the process of abnormal apoptosis, it is hoped will improve fertility in patients with endometriosis. This has been demonstrated in the study by Johari[8], which found positive effects of supplementation of curcumin in mice model of endometriosis with the acquisition of fertilization success rates higher than placebo in terms of the number of ova and the ability of oocytes to complete the meiosis process. In the group given supplements of curcumin obtained a mean number of ova 15.42 ± 3.17 compared with the placebo group the mean number of ova 8.21 ± 2.82 (p = 0.0001).

These results may explain our study in which oocytes alleged role in the regulation of AMH by granulosa cells. The expression of AMH by granulosa cells is reduced when performed oositektomi and increased again when oocytes were cultured granulosa cells back together. The research studied the effect of curcumin on levels of AMH until now has not been reported. Our research has shown that the obtained serum AMH levels are higher in the group receiving curcumin supplementation, but further research needs to better understand the mechanisms underlying these findings.

CONCLUSION

Serum AMH levels in rat model of endometriosis who received curcumin supplementation is higher than placebo

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